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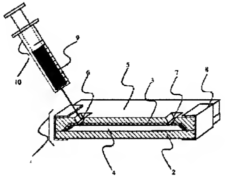
(54) **ANALYTIC ELEMENT**

(57) Abstract:

PURPOSE: To measure the infrared absorption spectrum of a liquid sample with high accuracy and sensitivity by applying a substrate, having a groove deposited on the surface thereof with a thin metal film, tightly to another substrate and then introducing a sample into the groove.

CONSTITUTION: The analytic element 1 comprises a smooth substrate 2 and another substrate 5 having a groove 4 deposited, on the surface thereof, with a thin metal film 3. The substrate 2 is made of a material having refractive index higher than that of a sample or the atmosphere and transparent in the infrared region, e.g. Al_2O_3 or MgO. The substrate 5 is made of silicon and provided with a groove 4 of predetermined depth, a sample introduction port 6, and an air vent 7 by photolithography and etching. The substrates 2, 5 are tightened by means of a clip 8. A sample 9 is introduced through the sample introduction port 6 into the groove 4 through capillarity using a syringe 10, for example. The air is discharged from the groove to the outside through the air vent 7. Since the depth of groove is just equal to the length of optical path length in the sample, highly accurate analysis is realized using an optical path of short length.



DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Industrial Application]This invention relates to the sample cell which measures the infrared absorption spectrum of a viscous low liquid sample.
[0002]
[Description of the Prior Art]In "the materials analysis (from 69 pages to **** Koichi, the Iwamoto ******, (1986), Kodansha SAIENTIFIKU, and 71 pages) by an infrared method", the transmission type conventional liquid sample cell is described. Here, the fixed direct vent type liquid cell to which the capillary film method, the window material, spacer, and frame which sandwich a sample between the window materials of two sheets, and adjust thickness by a lockscrew are being fixed using adhesives, and the liquid cell of the assembly type are described.
[0003]The measuring device of general attenuated total reflection spectroscopy is described in the above-mentioned writing "materials analysis (from 106 pages to 107 pages) by an infrared method."
[0004]The high sensitivity infrared absorption spectrometry using a total reflection prism and metal is discussed in "the 42nd volume of applied spectroscopy (1988), and the 1296th page to the 1302nd page." Here, measurement is performed with the composition of Otto (Otto) arrangement called a prism sample-metal thin film. The thin film of the polyvinyl acetate which is a sample is formed on prism, and also it is measuring by vapor-depositing silver in thickness of 20 nm on it using the prism of germanium. Measurement by the former 5 times the signal to noise ratio of the result is enabled.
[0005]The example which carried out high sensitivity measurement of the molecule in solution is stated to "623 pages" from the 158th volume of a surface science (1985), and the 616th page. Here, high sensitivity detection of the mercaptobenzothiazole (MBT) dissolved into aqueous acids is measured by KURECHUMAN (Kretschmann) arrangement of the composition of a prism metal-sample using the total reflection prism which vapor-deposited silver. It is suggested from the peak of the C=S stretching vibration of MBT

disappearing and the peak of Ag(I) MBT increasing instead that the local field leading to infrared-absorption increase of Kretschmann arrangement attains to only the distance about [which is sticking to the vapor-deposited silver] a molecular layer.

[0006]

[Problem(s) to be Solved by the Invention]Conventionally, since control of the thickness of a sample was difficult and light path length was not constant, the reproducibility of measurement was not able to use bad the fluid, especially the infrared absorption spectrum measured with the penetration method of solution for the quantitative analysis. The maintenance of washing of a cell, an assembly, etc. was complicated. The high sensitivity infrared absorption spectrometry using the metal thin film and total reflection prism which have been performed conventionally is mainly a thing for a solid sample, and the example of measurement for solution was restricted to Kretschmann arrangement.

[0007]The cause of the infrared-absorption increase by measurement of the Kretschmann arrangement which made this solution the sample, The distance which the surface electric field which it was presupposed that it was increase of the surface electric field by the localization plasmon excited when light enters into the metal particles which constitute a metal thin film, and increased attains to is guessed from about several nanometers and an experimental result. Therefore, the molecule in solution had a chemical interaction to metal, it is required for increase of infrared absorption for the adsorption layer of a measuring object molecule to exist near the metal thin film which a local field produces, and analysis of the stable molecule was not completed chemically.

[0008]On the other hand, in Otto arrangement, nonradioactive surface plasmon resonance excited when light enters into a metal membrane at a certain fixed angle is made into the cause of infrared-absorption increase, but as mentioned above, there is no example of measurement in solution. Although it was required in Otto arrangement to enter light in a metal thin film via a sample layer from the prism side, since the exudation of the light from the prism to the sample side was about several mere micrometers, it was difficult to install a fluid on prism thinly in this way. Therefore, high sensitivity measurement of solution was not able to be performed in the infrared-spectrum measuring method which combined conventional metal and prism.

[0009]

[Means for Solving the Problem]In order to solve the above-mentioned problem, a slot is formed by a photolithography and etching, A substrate in which a metal thin film was formed to a groove surface was stuck to another substrate, an opening for introducing a sample was provided, and it had composition which introduces a sample all over a slot, and was considered as an analysis cartridge which controls thickness of a sample by a tooth depth. In order to measure an infrared absorption spectrum to high sensitivity, a metal thin film was formed in a groove surface.

[0010]

[Function]The above-mentioned means acts as follows. The tooth depth of the second

substrate can prescribe the thickness of the sample held on the first substrate by sticking the second substrate in which the slot was formed to the first substrate, and making it the cell constitution which fills up the slot of the second substrate with a sample. A tooth depth can be controlled by mum order and by using etching for groove formation can prescribe the thickness of a sample very thinly. In the infrared-absorption-spectrum measurement in a penetration method, a tooth depth serves as light path length in the inside of a sample as it is, and the molecule which melted into the large solvent of infrared absorption, such as water, can be analyzed with sufficient accuracy by measuring by very short light path length.

[0011]The light which permeates and comes out of the substrate for optical waveguides reaches to the metal thin film surface formed in the groove surface via the sample, and makes a surface of metal excite surface plasmon resonance by forming a sample layer very thinly in the high sensitivity infrared-absorption-spectrum measurement by the attenuated total reflection spectroscopy using a metal thin film. The surface plasmon resonance of a surface of metal increases the infrared absorption of the sample which touches metal, and can measure a infrared spectrum to high sensitivity. By a semiconductor process etc., since it can mass-produce, this analysis element can be used as a disposable cell, and the complicated maintenance of washing of a cell, etc. is unnecessary.

[0012]

[Example]Drawing 1 is an explanatory view showing the analysis element of the first example of this invention. This analysis element 1 comprises two substrates, the first smooth substrate 2 and the second substrate 5 that installed the slot 4 which formed the metal thin film 3 in the surface by vacuum evaporation. The first substrate 2 has refractive indicees larger than a sample and the atmosphere, such as aluminum$_2$O$_3$, MgO, ZnSe, Si, and germanium, and transparent construction material is used for an infrared region. The second substrate 5 comprises silicon.

The sample feed port 6 and the degasification mouth 7 which are the predetermined sample installation groove 4 and penetrating port of the depth (this example 0.5 micrometer) are formed by a photolithography and etching.

Since silicon etching is used for processing of the sample installation groove 4, the depth control by mum order is possible. The first substrate 2 and the second substrate 5 are stuck by pressure with the clip 8.

[0013]The sample 9 is introduced by capillarity all over the slot 4 from the sample feed port 6 in syringe 10 grade. The air in the slot 4 is then discharged out of a slot from the degasification mouth 7.

[0014]Drawing 2 and drawing 3 are the sectional views of the analysis elements 11 and 12 which make a sample the solution of the second and third example of this invention. The analysis element 11 shown in drawing 2 forms the oxide film 13 in the adhesion side surface of the gold thin film 3 and the sample feed port 6 surface which were vapor-deposited to the second substrate 5 of the analysis element 1 shown in drawing 1, and the

second substrate of the first substrate 2 by ion weld slag. The material surfaces used as the construction material of substrates, such as silicon and zinc selenide, are character which is easy to flip water by hydrophobicity. Therefore, the sample induction surface can be made into hydrophilic nature with an oxide film, and a sample can be promptly developed all over the sample installation groove 4.

[0015]The analysis element 12 shown in drawing 3 is what filled up slot 4 portion of the analysis element 1 shown in drawing 1 with the particles 14 of absorptivity substances, such as cellulose, and can introduce a sample all over the slot 4 promptly by work of the absorptivity particles 14.

[0016]Drawing 4 is a measurement gestalt of the infrared absorption spectrum of the solution by the penetration method using the analysis element 1 shown in drawing 1. In the sample chamber of infrared spectrometer, the analysis element 1 is installed so that the sample layer 9 in the slot 4 may become vertical to the infrared light 16 with the holder 15. The depth of the slot 4 of this analysis element 1 is 0.5 micrometer. This depth becomes the thickness of the sample 9, i.e., the light path length in a sample, as it is. Since this analysis element can be mass-produced by a semiconductor process etc., it can be cheap, the error between elements can use it as few disposable elements, and the troublesomeness of washing like the conventional transmission type sample cell or sample exchange can be measured by there being nothing. It is lost by making contamination of a sample disposable.

[0017]Drawing 5 is a measurement gestalt of the infrared absorption spectrum of the solution by the attenuated total reflection spectroscopy using the analysis element 1 shown in drawing 1. Since light volume sufficient in order to excite the surface plasmon resonance leading to high-sensitivity-izing of infrared absorption for the high sensitivity measurement by the analysis element 1 is required, the bright Fourier-transform-infrared-spectroscopy meter and infrared laser of an optical system are used for the analysis apparatus etc. which were used as the light source. The analysis element 1 is installed in the holder 20 which offered the prism 19 for outgoing radiation for emitting to a detector the infrared light which has spread the prism 18 for incidence and the first substrate for entering the infrared light 16 from the light source 17 into the first substrate 2 used as an optical waveguide. This holder 20 is installed in a sample chamber, and the analysis element has become an insertion type to the holder. The analysis element 1 is demounted from a holder in the case of sample exchange, and the exchange of it has become possible [whole element].

[0018]The infrared light 16 emitted from the light source 17 turns into p-polarized light through the light polarizer 21, and enters into the prism 18 near the critical angle of prism. Infrared light causes diffraction on the square of the prism 18, enters into the first substrate 2 of the analysis element 1 which touched the prism 18, it reaches the prism 19 for outgoing radiation, carrying out the multiple echo of the inside of a substrate, and is emitted to a detector with the prism 19. About 2-3 micrometers of lights which carried out total internal reflection to the first substrate 2 by the interface of the sample 9 sink in as an

evanescent wave into a sample.
[0019]the depth of the sample installation groove 4 of this analysis element -- 0.5 micrometer it is -- since -- an evanescent wave reaches the gold thin film 3, and surface plasmon resonance is excited. By this surface plasmon resonance, the infrared absorption in a sample increases and the infrared absorption spectrum of a sample can be measured to high sensitivity.
[0020]Drawing 6 is the general drawing of the blood sugar meter 22 which made the sample whole blood using the sensitive analysis element 1 shown in drawing 1. It has the printer 24 and the display 25 for outputting a temporal change of the keyboard 23 which inputs the data about the analysis element 1 and sample which trickle a sample with an installed type small analyzer, the blood sugar level measured with this device, and a patient's blood sugar level.
[0021]Drawing 7 is a block diagram of the blood sugar meter of drawing 6. The infrared light 27 emitted from the infrared light source 26 enters into the analysis element 1, has the light of a specified wavelength absorbed by the blood in an element, and is emitted to the interferometer 28. The light which produced phase contrast with the interferometer 28 is led to the detector 29, and is inputted into the computer 32 as the digital signal 31 through A/D converter 30.
[0022]A signal is changed into the absorbance for every wave number by the Fourier transform. The blood sugar level in a sample is computed by including the absorbance sequence of numbers of 1181-950 cm^{-1} of a sample in the measuring formula which calculated the blood sugar level and the relation of the absorbance sequence of numbers of 1181-950 cm^{-1} of a blood spectrum by the multivariate analysis beforehand. The computed blood sugar level is told to an operating personnel by the output devices 33, such as a display and a printer.
[0023]Drawing 8 is correlation with the conventional enzymatic process of the glucose measured with the blood sugar meter of this invention. The result was as good as gamma= 0.962. In this invention, reagent loess can perform measurement equivalent to the conventional enzymatic process.
[0024]
[Effect of the Invention]According to this invention, the infrared absorption spectrum of a liquid sample can be measured to high degree of accuracy and high sensitivity.

[Translation done.]

CLAIMS

[Claim(s)]
[Claim 1]In an optical cell which measures infrared absorption of a sample with attenuated total reflection spectroscopy or a penetration method, An analysis element controlling thickness of said sample by said tooth depth which stuck the first substrate and the second substrate that provided a slot which carried out the opening to said first substrate side, and formed a metal thin film in the surface, and said slot was filled up with a sample, and was filled up with said sample.
[Claim 2]An analysis element which said second substrate according to claim 1 carried out pattern NINGU of the shape of said slot by a photolithography, and formed a slot by etching.
[Claim 3]An analysis element which equipped said second substrate according to claim 1 with a sample feed port and a degasification mouth.
[Claim 4]An analysis element which said metal thin film becomes from gold, silver, copper, aluminum, and platinum in claim 1.
[Claim 5]An analysis element which embellished a hydrophilic group or oxide films, such as a hydroxyl group and an amino group, in claim 1 on the sample contact part part surface of said first substrate and said second substrate.
[Claim 6]An analysis element with which absorptivity particles, such as polyethylene oxide and polyamide, are filled up into a slot formed in said second substrate in claim 1.
[Claim 7]An analysis element in which said first substrate has an incidence mechanism of infrared light to inside of said first substrate, and an outgoing radiation mechanism of infrared light from said first substrate to a detector in claim 1, and said ON outgoing radiation mechanism is a diffraction grating, prism, or an optical fiber.
[Claim 8]An analysis element which said second substrate according to claim 1 becomes from silicon.
[Claim 9]Said first substrate according to claim 1 is the refractive index 1.4 of germanium, zinc selenide, silicon, etc. An analysis element which consists of a transparent crystal in an infrared region above.

[Claim 10]A hemanalysis device which uses said analysis element for infrared spectrometer with a computer department for processing a signal detected in an infrared light source, an interferometer, a detector, and said detector in claim 1 as a sample cell.

[Translation done.]